

O-连接糖基化 - 维基百科 --- O-linked glycosylation

W en.wikipedia.org/wiki/O-linked_glycosylation

Contributors to Wikimedia projects

O-linked glycosylation is the attachment of a sugar molecule to the oxygen atom of serine (Ser) or threonine (Thr) residues in a protein. **O-glycosylation** is a post-translational modification that occurs after the protein has been synthesised. In eukaryotes, it occurs in the endoplasmic reticulum, Golgi apparatus and occasionally in the cytoplasm; in prokaryotes, it occurs in the cytoplasm.^[1] Several different sugars can be added to the serine or threonine, and they affect the protein in different ways by changing protein stability and regulating protein activity. O-glycans, which are the sugars added to the serine or threonine, have numerous functions throughout the body, including trafficking of cells in the immune system, allowing recognition of foreign material, controlling cell metabolism and providing cartilage and tendon flexibility.^[2] Because of the many functions they have, changes in O-glycosylation are important in many diseases including cancer, diabetes and Alzheimer's. O-glycosylation occurs in all domains of life, including eukaryotes, archaea and a number of pathogenic bacteria including *Burkholderia cenocepacia*,^[3] *Neisseria gonorrhoeae*^[4] and *Acinetobacter baumannii*.^[5]

O-连接糖基化是糖分子与蛋白质中丝氨酸 (Ser) 或苏氨酸 (Thr) 残基的氧原子连接。O-糖基化是蛋白质合成后发生的翻译后修饰。在真核生物中，它出现在内质网、高尔基体中，偶尔也出现在细胞质中；在原核生物中，它发生在细胞质中。^[1] 丝氨酸或苏氨酸上可以添加几种不同的糖，它们通过改变蛋白质稳定性和调节蛋白质活性以不同的方式影响蛋白质。O-聚糖是添加到丝氨酸或苏氨酸中的糖，在全身具有多种功能，包括在免疫系统中运输细胞、识别异物、控制细胞新陈代谢以及提供软骨和肌腱的灵活性。^[2] 由于它们具有多种功能，O-糖基化的变化在许多疾病中非常重要，包括癌症、糖尿病和阿尔茨海默病。O-糖基化发生在生命的各个领域，包括真核生物、古细菌和许多病原菌，包括新洋葱伯克霍尔德菌、^[3] 淋病奈瑟菌^[4] 和鲍曼不动杆菌。^[5]

Common types of O-glycosylation

O-糖基化的常见类型

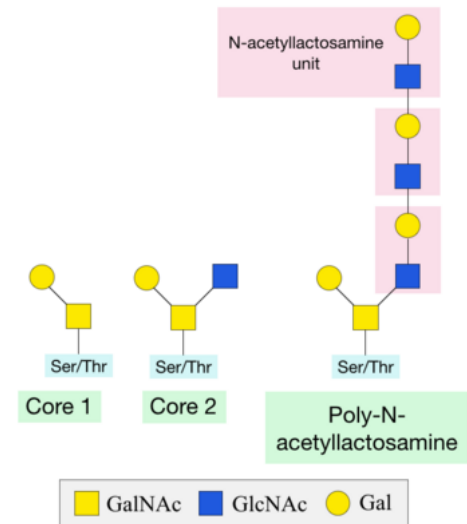
O-N-acetylgalactosamine (O-GalNAc)

O-N-乙酰半乳糖胺 (O-GalNAc)

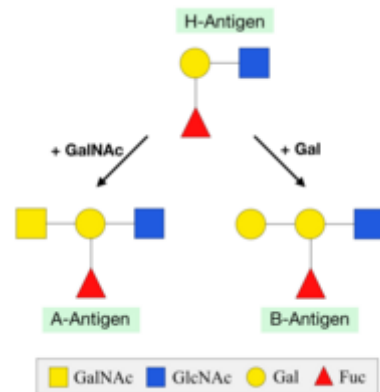
Addition of N-acetylgalactosamine (GalNAc) to a serine or threonine occurs in the Golgi apparatus, after the protein has been folded.^{[1][6]} The process is performed by enzymes known as GalNAc transferases (GALNTs), of which there are 20 different types.^[6] The initial O-GalNAc structure can be modified by the addition of other sugars, or other compounds such as methyl and acetyl groups.^[1] These modifications produce 8 core structures known to date.^[2] Different cells have different enzymes that can add further sugars, known as

glycosyltransferases, and structures therefore change from cell to cell.^[6] Common sugars added include galactose, *N*-acetylglucosamine, fucose and sialic acid. These sugars can also be modified by the addition of sulfates or acetyl groups.

蛋白质折叠后，N-乙酰半乳糖胺 (GalNAc) 与丝氨酸或苏氨酸的添加发生在高尔基体中。^[1]^[6] 该过程由称为 GalNAc 转移酶 (GALNT) 的酶执行，该酶有 20 种不同类型。^[6] 最初的 O-GalNAc 结构可以通过添加其他糖或其他化合物（如甲基和乙酰基）进行修饰。^[1] 这些修改产生了迄今为止已知的 8 个核心结构。^[2] 不同的细胞具有不同的酶，可以添加更多的糖，称为糖基转移酶，因此结构因细胞而异。^[6] 常见添加的糖类包括半乳糖、N-乙酰氨基葡萄糖、岩藻糖和唾液酸。这些糖也可以通过添加硫酸盐或乙酰基进行修饰。



Common O-GalNAc core structures; Core 1, Core 2 and poly-N-acetyllactosamine structures. 常见的O-GalNAc核心结构；核心 1、核心 2 和聚-N-乙酰基乳糖胺结构。



N-acetylgalactosamine (GalNAc) can be added to the H-antigen to form the A-antigen. Galactose (Gal) can be added to form the B-antigen.

N-乙酰半乳糖胺 (GalNAc) 可以添加到H-抗原中形成A-抗原。可以添加半乳糖 (Gal) 以形成 B 抗原。

Biosynthesis 生物合成

GalNAc is added onto a serine or threonine residue from a precursor molecule, through the activity of a GalNAc transferase enzyme.^[1] This precursor is necessary so that the sugar can be transported to where it will be added to the protein. The specific residue onto which GalNAc will be attached is not defined, because there are numerous enzymes that can add

the sugar and each one will favour different residues.^[7] However, there are often proline (Pro) residues near the threonine or serine.^[6]

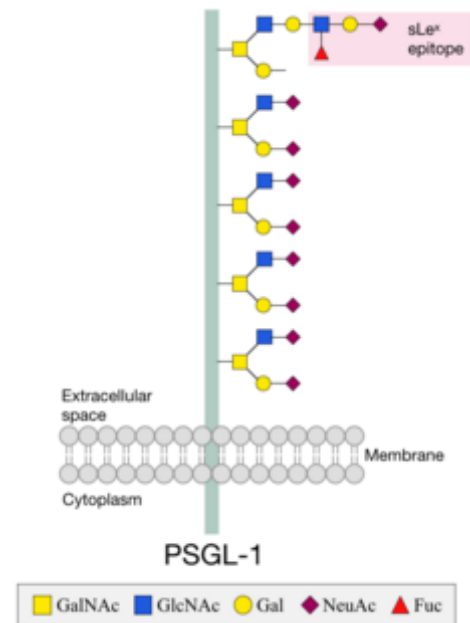
通过 GalNAc 转移酶的活性，将 GalNAc 添加到前体分子的丝氨酸或苏氨酸残基上。^[1] 这种前体是必需的，以便糖可以被运输到将其添加到蛋白质中的地方。GalNAc 所附着的具体残基尚未确定，因为有多种酶可以添加糖，并且每种酶都会偏向于不同的残基。^[7] 然而，苏氨酸或丝氨酸附近常常有脯氨酸 (Pro) 残基。^[6]

Once this initial sugar has been added, other glycosyltransferases can catalyse the addition of additional sugars. Two of the most common structures formed are Core 1 and Core 2. Core 1 is formed by the addition of a galactose sugar onto the initial GalNAc. Core 2 consists of a Core 1 structure with an additional *N*-acetylglucosamine (GlcNAc) sugar.^[6] A poly-*N*-acetylglucosamine structure can be formed by the alternating addition of GlcNAc and galactose sugars onto the GalNAc sugar.^[6]

一旦添加了初始糖，其他糖基转移酶就可以催化添加额外的糖。最常见的两种结构是核心 1 和核心 2。核心 1 是通过在初始 GalNAc 上添加半乳糖而形成的。核心 2 由核心 1 结构和额外的 *N*-乙酰氨基葡萄糖 (GlcNAc) 糖组成。^[6] 通过在 GalNAc 糖上交替添加 GlcNAc 和半乳糖，可以形成聚-*N*-乙酰基乳糖胺结构。^[6]

Terminal sugars on O-glycans are important in recognition by lectins and play a key role in the immune system. Addition of fucose sugars by fucosyltransferases forms Lewis epitopes and the scaffold for blood group determinants. Addition of a fucose alone creates the H-antigen, present in people with blood type O.^[6] By adding a galactose onto this structure, the B-antigen of blood group B is created. Alternatively, adding a GalNAc sugar will create the A-antigen for blood group A.

O-聚糖上的末端糖对于凝集素的识别很重要，并且在免疫系统中发挥着关键作用。通过岩藻糖基转移酶添加岩藻糖形成路易斯表位和血型决定簇的支架。单独添加岩藻糖即可产生 H 抗原，存在于 O 型血的人中。^[6] 通过在该结构上添加半乳糖，可产生 B 型血的 B 抗原。或者，添加 GalNAc 糖将产生 A 型血的 A 抗原。



PSGL-1 has several O-glycans to extend the ligand away from the cell surface. An sLe^x epitope allows interactions with the receptor for leukocyte localisation.

PSGL-1 具有多个 O-聚糖，可将配体延伸至远离细胞表面的位置。sLe^x 表位允许与白细胞定位受体相互作用。

Functions 功能

O-GalNAc sugars are important in a variety of processes, including leukocyte circulation during an immune response, fertilisation, and protection against invading microbes.^{[1][2]}

O-GalNAc 糖在多种过程中都很重要，包括免疫反应期间的白细胞循环、受精和防止微生物入侵。^{[1] [2]}

O-GalNAc sugars are common on membrane glycoproteins, where they help increase rigidity of the region close to the membrane so that the protein extends away from the surface.^[6] For example, the low-density lipoprotein receptor (LDL) is projected from the cell surface by a region rigidified by O-glycans.^[2]

O-GalNAc 糖在膜糖蛋白上很常见，它们有助于增加靠近膜的区域的刚性，从而使蛋白质远离表面延伸。^[6] 例如，低密度脂蛋白受体 (LDL) 通过 O-聚糖硬化的区域从细胞表面突出。^[2]

In order for leukocytes of the immune system to move into infected cells, they have to interact with these cells through receptors. Leukocytes express ligands on their cell surface to allow this interaction to occur.^[1] P-selectin glycoprotein ligand-1 (PSGL-1) is such a ligand, and contains a lot of O-glycans that are necessary for its function. O-glycans near the membrane maintain the elongated structure and a terminal sLe^x epitope is necessary for interactions with the receptor.^[8]

为了使免疫系统的白细胞进入受感染的细胞，它们必须通过受体与这些细胞相互作用。白细胞在其细胞表面表达配体以允许这种相互作用发生。^[1] P-选择素糖蛋白配体-1 (PSGL-1) 就是这样一种配体，含有大量其功能所必需的O-聚糖。膜附近的 O-聚糖维持伸长的结构，并且末端 sLe^x 表位对于与受体相互作用是必需的。^[8]

Mucins are a group of heavily O-glycosylated proteins that line the gastrointestinal and respiratory tracts to protect these regions from infection.^[6] Mucins are negatively charged, which allows them to interact with water and prevent it from evaporating. This is important in their protective function as it lubricates the tracts so bacteria cannot bind and infect the body. Changes in mucins are important in numerous diseases, including cancer and inflammatory bowel disease. Absence of O-glycans on mucin proteins changes their 3D shape dramatically and often prevents correct function.^{[1][9]}

粘蛋白是一组高度 O-糖基化的蛋白质，分布在胃肠道和呼吸道中，以保护这些区域免受感染。^[6] 粘蛋白带负电荷，这使得它们能够与水相互作用并防止水蒸发。这对于它们的保护功能很重要，因为它可以润滑肠道，使细菌无法结合和感染身体。粘蛋白的变化在许多疾病中都很重要，包括癌症和炎症性肠病。粘蛋白上缺少 O-聚糖会显著改变其 3D 形状，并且常常妨碍正常功能。^{[1] [9]}

O-N-acetylglucosamine (O-GlcNAc) **O-N-乙酰氨基葡萄糖 (O-GlcNAc)**

Main article: O-GlcNAc 主条目：O-GlcNAc

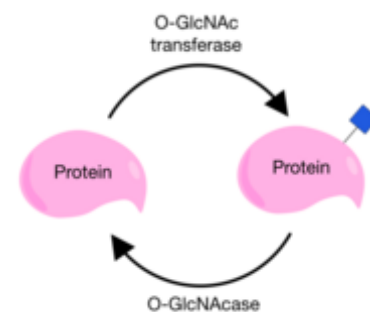
Addition of N-acetylglucosamine (O-GlcNAc) to serine and threonine residues usually occurs on cytoplasmic and nuclear proteins that remain in the cell, compared to O-GalNAc modifications which usually occur on proteins that will be secreted.^[10] O-GlcNAc modifications were only recently discovered, but the number of proteins with known O-GlcNAc modifications is increasing rapidly.^[7] It is the first example of glycosylation that does not occur on secretory proteins.

与通常发生在分泌的蛋白质上的 O-GalNAc 修饰相比，向丝氨酸和苏氨酸残基添加 N-乙酰氨基葡萄糖 (O-GlcNAc) 通常发生在保留在细胞中的细胞质和核蛋白质上。^[10] O-GlcNAc 修饰最近才被发现，但已知具有 O-GlcNAc 修饰的蛋白质数量正在迅速增加。^[7] 这是分泌蛋白上不发生糖基化的第一个例子。

O-GlcNAcylation differs from other O-glycosylation processes because there are usually no sugars added onto the core structure and because the sugar can be attached or removed from a protein several times.^{[6][7]} This addition and removal occurs in cycles and is performed by two very specific enzymes. O-GlcNAc is added by O-GlcNAc transferase (OGT) and removed by O-GlcNAcase (OGA). Because there are only two enzymes that affect this specific modification, they are very tightly regulated and depend on a lot of other factors.^[11] O-GlcNA 酰化与其他 O-糖基化过程不同，因为核心结构上通常不添加糖，而且糖可以多次从蛋白质上附着或去除。^{[6] [7]} 这种添加和去除循环发生，并由两种非常特殊的酶执行。O-GlcNAc 由 O-GlcNAc 转移酶 (OGT) 添加并由 O-GlcNAcase (OGA) 去除。由于只有两种酶会影响这种特定的修饰，因此它们受到非常严格的监管并取决于许多其他因素。^[11]

Because O-GlcNAc can be added and removed, it is known as a dynamic modification and has a lot of similarities to phosphorylation. O-GlcNAcylation and phosphorylation can occur on the same threonine and serine residues, suggesting a complex relationship between these modifications that can affect many functions of the cell.^{[6][12]} The modification affects processes like the cells response to cellular stress, the cell cycle, protein stability and protein turnover. It may be implicated in neurodegenerative diseases like Parkinson's and late-onset Alzheimer's^{[1][12]} and has been found to play a role in diabetes.^[13]

由于O-GlcNAc可以添加和去除，因此被称为动态修饰，与磷酸化有很多相似之处。O-GlcNAc 酰化和磷酸化可以发生在相同的苏氨酸和丝氨酸残基上，表明这些修饰之间存在复杂的关系，可以影响细胞的许多功能。^{[6] [12]} 这种修饰会影响细胞对细胞应激的反应、细胞周期、蛋白质稳定性和蛋白质周转等过程。它可能与帕金森氏症和迟发性阿尔茨海默氏症等神经退行性疾病有关^{[1] [12]}，并且已被发现在糖尿病中发挥作用。^[13]



O-GlcNAc is added to the protein by O-GlcNAc transferase and is removed by O-GlcNAcase in a continuous cycle.

O-GlcNAc 通过 O-GlcNAc 转移酶添加到蛋白质中，并在连续循环中被 O-GlcNAcase 去除。

Additionally, O-GlcNAcylation can enhance the Warburg Effect, which is defined as the change that occurs in the metabolism of cancer cells to favour their growth.^{[6][14]} Because both O-GlcNAcylation and phosphorylation can affect specific residues and therefore both have important functions in regulating signalling pathways, both of these processes provide interesting targets for cancer therapy.

此外，O-GlcNAcylation 可以增强 Warburg 效应，该效应被定义为癌细胞代谢中发生的有利于其生长的变化。^{[6] [14]} 由于O-GlcNAcNA酰化和磷酸化都可以影响特定残基，因此两者在调节信号通路中都具有重要功能，因此这两个过程都为癌症治疗提供了有趣的靶点。

O-Mannose (O-Man) O-甘露糖 (O-Man)

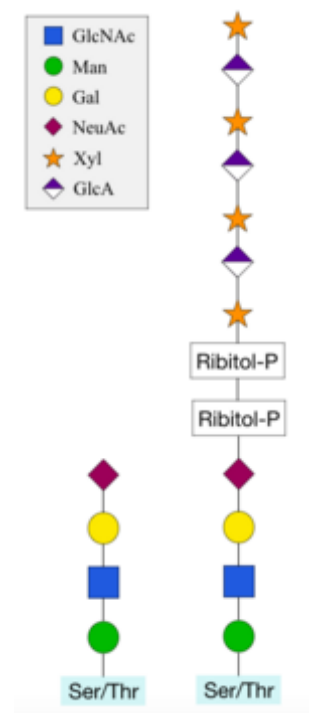
O-mannosylation involves the transfer of a mannose from a dolichol-*P*-mannose donor molecule onto the serine or threonine residue of a protein.^[15] Most other O-glycosylation processes use a sugar nucleotide as a donor molecule.^[7] A further difference from other O-glycosylations is that the process is initiated in the endoplasmic reticulum of the cell, rather than the Golgi apparatus.^[1] However, further addition of sugars occurs in the Golgi.^[15]

O-甘露糖基化涉及将甘露糖从多甘醇-P-甘露糖供体分子转移到蛋白质的丝氨酸或苏氨酸残基上。^[15] 大多数其他 O-糖基化过程使用糖核苷酸作为供体分子。^[7] 与其他 O-糖基化的另一个区别是，该过程是在细胞的内质网中启动的，而不是在高尔基体中启动的。^[1] 然而，糖的进一步添加发生在高尔基体中。^[15]

Until recently, it was believed that the process is restricted to fungi, however it occurs in all domains of life; eukaryotes, (eu)bacteria and archae(bacteri)a.^[16] The best characterised O-mannosylated human protein is α -dystroglycan.^[15] O-Man sugars separate two domains of

the protein, required to connect the extracellular and intracellular regions to anchor the cell in position.^[17] Ribitol, xylose and glucuronic acid can be added to this structure in a complex modification that forms a long sugar chain.^[8] This is required to stabilise the interaction between α -dystroglycan and the extracellular basement membrane. Without these modifications, the glycoprotein cannot anchor the cell which leads to congenital muscular dystrophy (CMD), characterised by severe brain malformations.^[15]

直到最近，人们还认为这一过程仅限于真菌，但它发生在生命的所有领域。真核生物、(EU)细菌和古细菌(bacteria)。^[16] 特征最明确的O-甘露糖基化人类蛋白是 α -dystroglycan。^[15] O-Man 糖将蛋白质的两个结构域分开，这是连接细胞外和细胞内区域以将细胞锚定到位所必需的。^[17] 核糖醇、木糖和葡萄糖醛酸可以通过复杂的修饰添加到该结构中，形成长糖链。^[8] 这是稳定 α -肌营养不良聚糖和细胞外基底膜之间相互作用所必需的。如果没有这些修饰，糖蛋白就无法锚定细胞，从而导致先天性肌营养不良症 (CMD)，其特征是严重的脑畸形。^[15]



O-Mannose sugars attached to serine and threonine residues on α -dystroglycan separate the two domains of the protein. Addition of Ribitol-P, xylose and glucuronic acid forms a long sugar that can stabilise the interaction with the basement membrane.

附着在 α -肌营养不良聚糖上丝氨酸和苏氨酸残基上的 O-甘露糖将蛋白质的两个结构域分开。添加Ribitol-P、木糖和葡萄糖醛酸形成长糖，可以稳定与基底膜的相互作用。

O-Galactose (O-Gal) O-半乳糖 (O-Gal)

O-galactose is commonly found on lysine residues in collagen, which often have a hydroxyl group added to form hydroxylysine. Because of this addition of an oxygen, hydroxylysine can then be modified by O-glycosylation. Addition of a galactose to the hydroxyl group is initiated in the endoplasmic reticulum, but occurs predominantly in the Golgi apparatus and only on hydroxylysine residues in a specific sequence.^{[1][18]}

O-半乳糖通常存在于胶原蛋白的赖氨酸残基上，胶原蛋白中通常添加羟基以形成羟赖氨酸。由于添加了氧，羟基赖氨酸可以通过 O-糖基化进行修饰。半乳糖与羟基的加成在内质网中起始，但主要发生在高尔基体中，并且仅以特定顺序发生在羟赖氨酸残基上。 [1] [18]

While this O-galactosylation is necessary for correct function in all collagens, it is especially common in collagen types IV and V.[19] In some cases, a glucose sugar can be added to the core galactose.[7]

虽然这种 O-半乳糖基化对于所有胶原蛋白的正确功能都是必需的，但它在 IV 型和 V 型胶原蛋白中尤其常见。 [19] 在某些情况下，可以将葡萄糖添加到核心半乳糖中。 [7]

O-Fucose (O-Fuc) O-岩藻糖 (O-Fuc)

Addition of fucose sugars to serine and threonine residues is an unusual form of O-glycosylation that occurs in the endoplasmic reticulum and is catalysed by two fucosyltransferases.[20] These were discovered in *Plasmodium falciparum*[21] and *Toxoplasma gondii*. [22]

将岩藻糖添加到丝氨酸和苏氨酸残基上是一种不寻常的 O-糖基化形式，发生在内质网中，并由两种岩藻糖基转移酶催化。 [20] 这些是在恶性疟原虫 [21] 和弓形虫中发现的。 [22]

Several different enzymes catalyse the elongation of the core fucose, meaning that different sugars can be added to the initial fucose on the protein.[20] Along with O-glucosylation, O-fucosylation is mainly found on epidermal growth factor (EGF) domains found in proteins.[7] O-fucosylation on EGF domains occurs between the second and third conserved cysteine residues in the protein sequence.[1] Once the core O-fucose has been added, it is often elongated by addition of GlcNAc, galactose and sialic acid.

几种不同的酶催化核心岩藻糖的延伸，这意味着可以将不同的糖添加到蛋白质上的初始岩藻糖上。 [20] 除了 O-葡萄糖基化之外，O-岩藻糖基化主要存在于蛋白质中的表皮生长因子 (EGF) 结构域中。 [7] EGF 结构域上的 O-岩藻糖基化发生在蛋白质序列中的第二个和第三个保守半胱氨酸残基之间。 [1] 一旦添加了核心 O-岩藻糖，通常会通过添加 GlcNAc、半乳糖和唾液酸来延长它。

Notch is an important protein in development, with several EGF domains that are O-fucosylated.[23] Changes in the elaboration of the core fucose determine what interactions the protein can form, and therefore which genes will be transcribed during development. O-fucosylation might also play a role in protein breakdown in the liver.[1]

Notch 是发育中的重要蛋白质，具有多个 O-岩藻糖基化的 EGF 结构域。 [23] 核心岩藻糖加工过程中的变化决定了蛋白质可以形成什么样的相互作用，从而决定了哪些基因将在发育过程中被转录。 O-岩藻糖基化也可能在肝脏中的蛋白质分解中发挥作用。 [1]

O-Glucose (O-Glc) O-葡萄糖 (O-Glc)

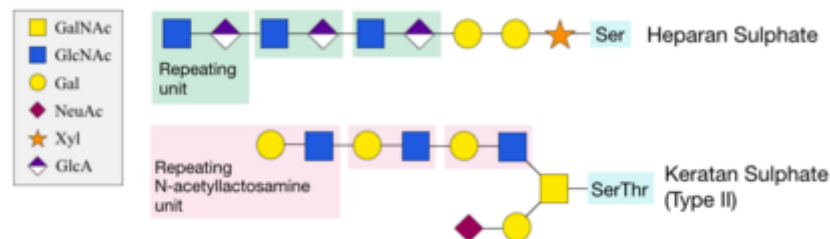
Similarly to O-fucosylation, O-glucosylation is an unusual O-linked modification as it occurs in the endoplasmic reticulum, catalysed by O-glucosyltransferases, and also requires a defined sequence in order to be added to the protein. O-glucose is often attached to serine residues between the first and second conserved cysteine residues of EGF domains, for example in clotting factors VII and IX.^[7] O-glucosylation also appears to be necessary for the proper folding of EGF domains in the Notch protein.^[24]

与 O-岩藻糖基化类似，O-葡萄糖基化是一种不寻常的 O-连接修饰，因为它发生在内质网中，由 O-葡萄糖基转移酶催化，并且还需要确定的序列才能添加到蛋白质中。O-葡萄糖通常附着在 EGF 结构域的第一个和第二个保守半胱氨酸残基之间的丝氨酸残基上，例如在凝血因子 VII 和 IX 中。^[7] O-葡萄糖基化似乎对于 Notch 蛋白中 EGF 结构域的正确折叠也是必要的。^[24]

Proteoglycans 蛋白多糖

Main article: [Proteoglycans](#)

主条目：蛋白多糖



Structures of heparan sulphate and keratan sulphate, formed by the addition of xylose or GalNAc sugars, respectively, onto serine and threonine residues of proteins.

硫酸乙酰肝素和硫酸角质素的结构，分别通过在蛋白质的丝氨酸和苏氨酸残基上添加木糖或 GalNAc 糖而形成。

Proteoglycans consist of a protein with one or more sugar side chains, known as glycosaminoglycans (GAGs), attached to the oxygen of serine and threonine residues.^[25] GAGs consist of long chains of repeating sugar units. Proteoglycans are usually found on the cell surface and in the extracellular matrix (ECM), and are important for the strength and flexibility of cartilage and tendons. Absence of proteoglycans is associated with heart and respiratory failure, defects in skeletal development and increased tumor metastasis.^[25]

蛋白聚糖由具有一个或多个糖侧链的蛋白质组成，称为糖胺聚糖 (GAG)，附着在丝氨酸和苏氨酸残基的氧上。^[25] GAG 由重复糖单元的长链组成。蛋白多糖通常存在于细胞表面和细胞外基质 (ECM) 中，对于软骨和肌腱的强度和灵活性很重要。蛋白多糖的缺乏与心脏和呼吸衰竭、骨骼发育缺陷和肿瘤转移增加有关。^[25]

Different types of proteoglycans exist, depending on the sugar that is linked to the oxygen atom of the residue in the protein. For example, the GAG heparan sulphate is attached to a protein serine residue through a xylose sugar.^[7] The structure is extended with several *N*-acetylglucosamine repeating sugar units added onto the xylose. This process is unusual and

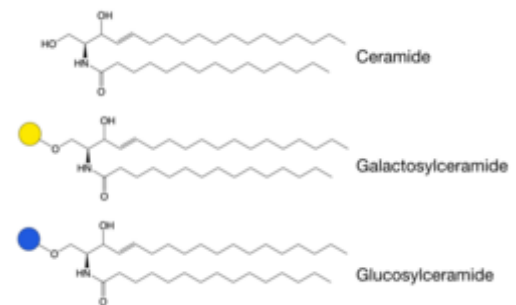
requires specific xylosyltransferases.^[6] Keratan sulphate attaches to a serine or threonine residue through GalNAc, and is extended with two galactose sugars, followed by repeating units of glucuronic acid (GlcA) and GlcNAc. Type II keratan sulphate is especially common in cartilage.^[25]

存在不同类型的蛋白多糖，具体取决于与蛋白质残基的氧原子相连的糖。例如，GAG 硫酸乙酰肝素通过木糖附着在蛋白质丝氨酸残基上。^[7] 通过添加到木糖上的几个 N-乙酰基乳糖胺重复糖单元来扩展结构。这个过程很不寻常，需要特定的木糖基转移酶。^[6] 硫酸角质素通过 GalNAc 附着在丝氨酸或苏氨酸残基上，并用两个半乳糖延伸，然后是葡萄糖醛酸 (GlcA) 和 GlcNAc 的重复单元。II 型硫酸角质素在软骨中尤其常见。^[25]

Lipids 脂质

Galactose or glucose sugars can be attached to a hydroxyl group of ceramide lipids in a different form of O-glycosylation, as it does not occur on proteins.

^[6] This forms glycosphingolipids, which are important for the localisation of receptors in membranes.^[8] Incorrect breakdown of these lipids leads to a group of diseases known as sphingolipidoses, which are often characterised by neurodegeneration and developmental disabilities. 半乳糖或葡萄糖可以以不同形式的 O-糖基化连接到神经酰胺脂质的羟基上，因为它不会发生在蛋白质上。^[6] 这会形成鞘糖脂，这对于膜中受体的定位很重要。^[8] 这些脂质的不正确分解会导致一组称为鞘脂沉积症的疾病，其特征通常是神经变性和发育障碍。



Structure of ceramide, galactosylceramide and glucosylceramide.

神经酰胺、半乳糖神经酰胺和葡萄糖神经酰胺的结构。

Because both galactose and glucose sugars can be added to the ceramide lipid, we have two groups of glycosphingolipids. Galactosphingolipids are generally very simple in structure and the core galactose is not usually modified. Glucosphingolipids, however, are often modified and can become a lot more complex.

由于半乳糖和葡萄糖都可以添加到神经酰胺脂质中，因此我们有两组糖鞘脂。半乳糖鞘脂通常结构非常简单，核心半乳糖通常不被修饰。然而，鞘糖脂经常被修饰并且可能变得更加复杂。

Biosynthesis of galacto- and glucosphingolipids occurs differently.^[6] Glucose is added onto ceramide from its precursor in the endoplasmic reticulum, before further modifications occur in the Golgi apparatus.^[8] Galactose, on the other hand, is added to ceramide already in the Golgi apparatus, where the galactosphingolipid formed is often sulfated by addition of sulfate groups.^[6]

半乳糖鞘脂和葡萄糖鞘脂的生物合成发生方式不同。^[6] 在高尔基体中发生进一步修饰之前，葡萄糖从内质网中的前体添加到神经酰胺上。^[8] 另一方面，半乳糖被添加到高尔基体中的神经酰胺中，其中形成的半乳糖鞘脂通常通过添加硫酸基团而被硫酸化。^[6]

Glycogenin 糖原

One of the first and only examples of O-glycosylation on tyrosine, rather than on serine or threonine residues, is the addition of glucose to a tyrosine residue in glycogenin.^[7]

Glycogenin is a glycosyltransferase that initiates the conversion of glucose to glycogen, present in muscle and liver cells.^[26]

第一个也是唯一的酪氨酸（而不是丝氨酸或苏氨酸残基）O-糖基化的例子之一是将葡萄糖添加到糖原中的酪氨酸残基上。^[7] 糖原素是一种糖基转移酶，可启动葡萄糖转化为糖原，存在于肌肉和肝细胞中。^[26]

Clinical significance 临床意义

All forms of O-glycosylation are abundant throughout the body and play important roles in many cellular functions.

所有形式的 O-糖基化在体内大量存在，并在许多细胞功能中发挥重要作用。

Lewis epitopes are important in determining blood groups, and allow the generation of an immune response if we detect foreign organs. Understanding them is important in organ transplants.^[1]

刘易斯表位对于确定血型很重要，并且如果我们检测到外来器官，则可以产生免疫反应。了解它们对于器官移植很重要。^[1]

Hinge regions of immunoglobulins contain highly O-glycosylated regions between individual domains to maintain their structure, allow interactions with foreign antigens and protect the region from proteolytic cleavage.^{[1][8]}

免疫球蛋白的铰链区在各个结构域之间包含高度 O-糖基化的区域，以维持其结构，允许与外源抗原相互作用并保护该区域免受蛋白水解切割。^{[1] [8]}

Alzheimer's may be affected by O-glycosylation. Tau, the protein that accumulates to cause neurodegeneration in Alzheimer's, contains O-GlcNAc modifications which may be implicated in disease progression.^[1]

阿尔茨海默病可能受到 O-糖基化的影响。Tau 蛋白是一种累积导致阿尔茨海默病神经变性的蛋白质，含有 O-GlcNAc 修饰，可能与疾病进展有关。^[1]

Changes in O-glycosylation are extremely common in cancer. O-glycan structures, and especially the terminal Lewis epitopes, are important in allowing tumor cells to invade new tissues during metastasis.^[6] Understanding these changes in O-glycosylation of cancer cells can lead to new diagnostic approaches and therapeutic opportunities.^[1]

O-糖基化的变化在癌症中极为常见。O-聚糖结构，尤其是末端路易斯表位，对于允许肿瘤细胞在转移过程中侵入新组织非常重要。^[6] 了解癌细胞 O-糖基化的这些变化可以带来新的诊断方法和治疗机会。^[1]